

TABLE 12-continued

0.00	73.29	73.29	406.8
1.26	73.29	74.55	606.8
6.30	73.29	79.59	1264
0.00	146.58	146.58	442.3
2.52	146.58	149.10	881.2
5.04	146.58	151.62	1992
0.00	293.16	293.16	450.4
2.52	293.16	295.68	1482
5.04	293.16	298.20	>2000
0.00	366.45	366.45	418.1
1.26	366.45	367.71	>2000
6.30	366.45	372.75	>2000
Minocycline ng/ml	Clindamycin ng/ml	Total ng/ml	ET50
0.00	0.00	0.00	434.8
1.26	0.00	1.26	637.6
2.52	0.00	2.52	1072
5.04	0.00	5.04	>2000
6.30	0.00	6.30	>2000
0.00	1.49	1.49	448.7
1.26	1.49	2.75	734.5
6.30	1.49	7.79	>2000
0.00	2.99	2.99	485.1
2.52	2.99	5.51	1227
5.04	2.99	8.03	>2000
0.00	5.97	5.97	521.1
2.52	5.97	8.49	1488
5.04	5.97	11.01	>2000
0.00	8.96	8.96	579.8
1.26	8.96	10.22	1650
6.30	8.96	15.26	>2000

[0213] Since the study included many possible combinations of two antibiotics, each with their own different concentration range, a matrix of possible antibiotic concentrations was designed, and degradation products of ORC were prepared accordingly (see Table 10). Since all the possible combinations could not be fitted into one 96 well plate, a series of MIC experiments were carried out. In order to compare between the different plates and obtain results which can provide information regarding the activity of the all antibiotics and concentrations tested, ET50 values (as described in Example 2) were used, which provided a quantitative measurement of the antibiotic activity which could be used to compare results from different assay plates.

[0214] Table 12 presents ET50 results for combinations of minocycline with rifampin or minocycline with clindamycin at different concentrations. The results show that 6.3 ng/ml minocycline in combination with 366.45 ng/ml rifampin (total 372.75 ng/ml antibiotic loaded), as well as 1.26 ng/ml minocycline in combination with 38.96 ng/ml clindamycin (total 10.22 ng/ml antibiotic loaded) is a sufficient level of antibiotics which provides a great antibiotic activity. In addition, a combination of 2.52 ng/ml minocycline with 293.16 ng/ml rifampin as well as 2.52 ng/ml minocycline with 0.5.97 ng/ml of clindamycin also provided a high level of antibiotic activity.

[0215] The primary stage study confirmed that no false positive antibacterial activity occurred, that the baseline antibacterial activity of the reagents and bacterial strains used was correct. The MIC obtained for *S. aureus* using a specific antibiotic alone was found to be consistent with values published in known literature.

[0216] In the secondary stage, it was shown that although it is reported that ORC itself has some intrinsic antimicrobial activity (Dineen P. "The effect of oxidized regenerated cellulose on experimental infected splenotomies" Journal of

Surgical Research 1977; 23: 114-116); the amount of ORC degradation products used in the present study was ineffective in providing bacterial growth inhibition as determined her MIC studies. The selected antibiotics were shown to exhibit different activity levels in the presence of degradation products of ORC. Specifically, rifampin and gentamycin activity was impaired by degradation products of ORC and MIC was increased; clindamycin and tetracycline activity showed no change in the presence of ORC and no change in MIC. However, surprisingly, only minocycline MIC was reduced when mixed with degradation products of ORC.

[0217] In the tertiary stage, degradation products of ORC pads impregnated with selected antibiotics including minocycline, rifampin and/or clindamycin were used. MIC results were found to be consistent with those of the secondary stage.

[0218] The levels of clindamycin required to be impregnated onto the ORC pad in order to achieve an inhibition of growth with degradation products of ORC were similar to those of the first stage MIC, i.e. there was no change of clindamycin antimicrobial activity. The levels of rifampin required to be impregnated onto the ORC pad used for production of degradation products of ORC in order to achieve an inhibition of growth were about 50 times higher than those of the first stage MIC i.e. the rifampin activity was impaired even when impregnated onto the ORC pad. Finally, the levels of minocycline required to be impregnated onto the ORC pad in order to achieve an inhibitory effect were about 20 times lower than those of the first stage MIC.

[0219] It was further found that when minocycline is impregnated onto an ORC pad in combination with an additional antibiotic, the ET50 was reduced for both minocycline and the additional antibiotic, i.e. either rifampin or clindamycin. As little as 1.26 ng/ml minocycline, together with 366.5 ng/ml rifampin or 8.9 ng/ml clindamycin were found to be sufficient for growth inhibition of *S. aureus*. The MIC for these antibiotics when used as single antibiotics in the absence of ORC (first stage MIC results) was found to be 250 ng/ml for minocycline, 62 ng/ml for clindamycin and 15 ng/ml for rifampin. These results prove a 200-fold reduction of the MIC for minocycline, and 6.8-fold reduction for clindamycin. Although the MIC for rifampin was higher than that seen as a single antibiotic, it remained less than that of the second stage MIC. Interestingly, even though minocycline is an antibiotic from the tetracycline family of antibiotics, the activity enhancement was restricted to minocycline and was not demonstrated for other members of the family (tetracycline).

[0220] The results demonstrate a synergistic effect for minocycline and degradation products of ORC. Degradation products obtained from a hemostatic ORC pad impregnated with a low concentration of minocycline are therefore able to provide a high level of antibiotic activity. The recommended antibiotic concentration for minocycline alone in an ORC pad is in the range of from 2.7 µg to 21.6 µg per gram ORC. When minocycline is used in combination with rifampin or clindamycin, the recommended antibiotic concentrations are from 0.5 µg to 2.7 µg minocycline per gram ORC together with from 31.4 µg to 157 µg rifampin per gram ORC or from 0.6 µg to 3.8 µg clindamycin per gram ORC.

1-10. (canceled)

11. A method for the treatment of an infection in a subject in need thereof, the method comprising administering to the